Claim Rejection Under 35 U.S.C. § 102

The Examiner rejected claims 1-10, 14, 16-18, 20 and 32 as being anticipated by Kuppe *et al., J. Bacteriol.* **17**:6077-6083 (1989). Specifically, the Examiner alleged that Kuppe "disclose(s)" the instantly claimed "composition comprising a purified or recombinantly produced phospholipase C enzyme of *B. cereus*. In addition, the Examiner alleged that Kuppe's composition is in form of a "liquid (culture medium of the host cell expressing the recombinant enzyme in milligram quantities) comprising a carrier such as beef extract or tryptone or NaCl which is recognized as a fed[e]d or food in the art."

Applicants respectfully traverse this rejection. In order to reject a claim under 35 U.S.C. § 102, the Examiner must demonstrate that each claim limitation is contained in a single prior art reference. *See Scripps Clinic & Research Foundation v. Genentech, Inc.,* 18 USPQ2d 1001, 1010 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.,* 231 USPQ 81, 90 (Fed. Cir. 1986). An allegedly anticipatory reference must enable the person of ordinary skill to practice the invention as claimed, otherwise the invention cannot be said to have been already within the public's possession, which is required for anticipation. *See Akzo, N.V. v. U.S.I.T.C.,* 1 USPQ2d 1241, 1245 (Fed. Cir. 1986); *In re Brown,* 141 USPQ 245, 249 (CCPA 1964).

A knowledgeable person would have to take into consideration the origin of a composition before he can orally administer Kuppe's composition to either a human or an animal. The phrases "physiologically acceptable carrier" and "suitable for oral administration" have a meaning, in light of the specification (see pages 12 and 13), that excludes the solutions described by Kuppe. The claimed compositions comprise an enzyme and a physiologically acceptable carrier for those enzymes. In addition, they are suitable for oral administration.

On the other hand, the Examiner seems to believe that Kuppe's composition, as described above, is in a form suitable for oral administration. In fact, Kuppe's composition is unsuitable for oral administration because it contains materials that are toxic and harmful to the recipient. Accordingly, Kuppe's compositions is different from the claimed invention. The present claims **exclude** constituents of the Kuppe's

Kuppe teaches cloning of phosphatidylinositol (PI)-specific phospholipase C (PLC) from *Bacillus cereus* into *Escherichia coli* and extraction of PI-PLC from an *E. coli* preparation via a single ammonium sulfate precipitation step. The administration of crude PI-PLC enzyme samples obtained by Kuppe's method is loaded with *E. coli* products including lipopolysaccharide (LPS) endotoxin. These products are harmful to both humans and animals. Accordingly, a knowledgeable reader would not consider Kuppe's enzyme preparation physiologically acceptable and suitable for oral formulation.

Kuppe is not a patentability-defeating reference because it fails to disclose a composition that is physiologically acceptable and suitable for oral administration, in the context of treating and lowering the risks of digestive tract infections. Indeed, Kuppe evidences no recognition of a therapeutic possibility for PLC. In fact, the inventors of the present application has noted that such therapeutic use of PI-PLC enzyme, administered orally as an anti-infection agent and be effective *in vivo,* has not been suggested in the prior art (see specification at page 10, line 31 to page 11, line 2). Accordingly, Kuppe fails to teach each and every element of the claimed invention. Reconsideration and withdrawal of the rejection under section 102 is respectfully requested.

Claim Rejection Under 35 U.S.C. § 103

The Examiner rejects claims 1-20 and 32 as being unpatentable over Kuppe *et al.* and Barbis *et al., Brazilian J. Med. Biol. Res.* **27**:401-407 (1994). Applicants respectfully traverse this rejection.

A proper rejection for obviousness under §103 requires consideration of two factors:

> (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition, or device, or carry out the claimed process and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure.

In re Vaeck, 947 F.2d 488, 493, 20 USPQ2d 1438 (Fed. Cir. 1991) [emphasis added].

The Examiner alleges that it "would have been obvious to one of ordinary skill in the art" to combine the teachings of Kuppe and Barbis to "fortify an animal feed such

that the animal consuming such feed would be imparted with a mechanism to avoid viral infection." Furthermore, the Examiner alleges that an ordinary artisan "would be motivated to reduce the dependency on drugs for treatments of such infections" and "would have a reasonable expectation of success" using the combined teachings of Kuppe and Barbis to practice the claimed invention.

The above-mentioned arguments presented to overcome the rejections over Kuppe are incorporated by reference in their entirety.

Barbis teaches that pretreatment of otherwise susceptible feline T cells with PI-PLC severely compromises the ability of canine parvovirus to infect the cells *in vitro*. Barbis does not teach the making of a PI-PLC formulation. Instead, Barbis obtains PI-PLC from commercial sources to study the mechanism of action of this enzyme in preventing canine parvovirus to bind to susceptible infected cells. In one experiment, PI-PLC was dissolved in dilute concentration with phosphate buffered saline (PBS). The amount of enzyme (in dilute concentration) in Barbis does not equate to the amount used in the claimed invention. Extremely diluted PI-PLC enzyme (2 U/mL) would not be suitable for oral formulation *in vivo*, as instantly claimed. Therefore, there is no reasonable expectation that the *in vitro* showing of PI-PLC action by Barbis would successfully work well *in vivo*. As with Kuppe, therefore, a knowledgeable reader informed by Barbis, would not have been prompted to orally administer a PI-PLC preparation, for treating or lowering the risk of digestive tract infections.

In summary, Kuppe and Barbis are not patentability-defeating references since they both fail to disclose compositions that are physiologically acceptable and suitable for oral administration in treating and lowering the risks of digestive tract infections. Accordingly, the Examiner has failed to make a case of *prima facie* obviousness. Applicants, therefore, respectfully request that the above rejection be withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, favorable reconsideration and allowance of this application are requested. An early notice in this regard is earnestly solicited. In the event that any issues remain, the Examiner is invited to contact the undersigned with any proposal to expedite prosecution.

Respectfully submitted,

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Should additional fees be necessary in connection with the filing of this paper, or if a petition for extension of time is required for timely acceptance of same, th Commissioner is hereby authorized to charge Deposit Account No. 19-0741 for any such fees; and applicant(s) hereby petition for any needed extension of time.

MARKED UP VERSION SHOWING CHANGES MADE

IN THE SPECIFICATION:

1. On page 18, lines 2-9, please replace the first full paragraph and replace it with the following in accordance with 37 C.F.R. § 1.121. A marked up version showing changes is attached:

The gene coding for phosphatidylinositol specific phospholipase C (PI-PLC) has been sequenced. See Kuppe *et al., J. Bacteriol.* **171**:6077-6083, 1989. Using PCR technology, the PI-PLC gene was cloned from *Bacillus cereus* (ATCC 6464) chromosomal DNA. An expression vector, pMEGA (BIO 101, Vista, CA), for *Bacillus megaterium* was used. Two PCR primers, [namely,] 5'-GACTAGTAATAAGAAGTTAATTTTG-3' (primer 1; SEQ ID NO:1) and 5'-CGGGATCCATATTGTTGGTTATTGG-3' (primer 2; SEQ ID NO:2), were designed with a *Spe*I site in primer-1 (SEQ ID NO:1) and a *Bam*HI site in primer-2 (SEQ ID NO:2).